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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,366	03/31/1998	GUDMUNDUR JOHANNSSON	0151/00211	6749

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	40

DATE MAILED: 06/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/050,366	JOHANNSSON ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 July 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENT, REMARKS AND STATUS OF THE CLAIMS

1. The amendment and remarks filed 1/27/03 are acknowledged, entered and considered. In view of Applicant's request claim 22 has been amended. Claims 22-24, 41 and 42 are now pending in the application. The rejection under 35 U.S.C. 103(a) over the prior art of record is withdrawn in view of Applicant's amendment, remarks and declaration filed under 37 C.F.R. 1.132.

2. The Finality of the previous Office action is also withdrawn in view of the following new grounds of rejections.

The following are new grounds of rejections:

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

3. Claims 22-24 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient having Metabolic Syndrome comprising Primary Insulin Resistance and abdominal/visceral obesity to decrease insulin resistance, wherein said method comprises administering to said patient recombinant human growth hormone (rhGH) in an amount effective for decreasing insulin resistance to said patient, does not reasonably provide enablement for treatment of a method comprising administering to said patient all kinds of growth hormones or functional derivatives thereof as claimed in

independent claim 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with independent claim 22.

The specification does not adequately teach the treatment and use of all kinds of growth hormones wherein the growth hormone comprises human growth hormone or a functional analog thereof or the growth hormone comprises human growth hormone as claimed in claims 22-24 and 42; rather, the specification teaches the use and/or administration of rhGH for treating a patient having Metabolic Syndrome to decrease insulin resistance as disclosed in Figures 1-3 and Tables 1-4 in the instant specification. Figures 1-3 and Tables 1-4 show that 9 months of rhGH treatment in middle-aged men with abdominal/visceral obesity reduced total body fat and resulted in specific and marked decrease of both abdominal, subcutaneous and visceral adipose tissue in comparison with placebo groups by the various assays disclosed in the Tables and Figures. However, the use of growth hormones in general for treatment purposes as claimed are not justified by the mere recitation/definition on page 3, lines 17-20 in the instant specification which states that the present invention thus relates to the use of growth hormone or analogues thereof as claimed the claims file (e.g., claim 22). By analog is meant a substance having the same biological activity as described here and having at least 65% homology with natural occurring growth hormone (i.e., which may encompass or include growth hormones from various species, such as bovine, porcine, equine, ovine, rodent, etc.). Thus, Applicant has not shown that

the various growth hormones defined in the specification and claimed would be effective as the exemplified rhGH formulations for the following reasons:

Applicant acknowledges in the instant specification on page 2, lines 14-19 that in spite of the replacement therapy with rhGH which demonstrated favorable effects on most of the features of GH deficiency in adults; however, there has never been investigation whether rhGH treatment can improve the metabolic abnormalities observed in abdominal/visceral obesity, except the instant invention uses randomized, double-blind, placebo-controlled design to evaluate the effects of rhGH administration in patients with abdominal/visceral obesity. Further, with respect to the dosage ranges, the instant specification on page 5, lines 5-12 states that the daily rhGH dose was 9.5 μg/kg (0.20 IU/kg body weight/week) administered subcutaneously and the dose was reduced by half in the event of side-effects. Thus, showing clearly the unpredictability of the dosage regimen even in the exemplified rhGH, let alone using all kinds of growth hormones for the claimed treatment.

Furthermore, the reference of Holly et al (J. Endocr., Volume 118, pp. 353-364, 1988) reviews the role of growth hormone in diabetic patients. The reference on page 357, right column shows the unpredictability of GH molecule in diabetic patient (i.e., Is the GH molecule itself different in diabetes?) because circulating GH is a heterogenous family of closely related peptides as examined by several investigators. Although, a number of GH molecule variants have been described, only two have been found in circulation in appreciable amount in man, these being the normal 22,000 Dalton (22 kDa) GH and a 20 kDa GH form differing from the

former by a 15 amino acid deletion produced by alternative splicing of GH mRNA. In addition, it is well recognized that circulating GH elutes from gel filtration columns in three size forms with molecular weights of approximately 22 kDa, 45 kDa and 80-90 kDa (known classically as GH, big-GH and big-big-GH, respectively). Thus, the GH molecule can vary with the nature of the protein, its source, and its binding conditions resulting in differences of immunological properties. Moreover, the reference of Salomon et al., (N. Engl. J. Med., Vol. 321, No. 26, pp. 1797-1803, Dec. 28, 1989) teaches the effects of treatment with rhGH on body composition and metabolism in adults with growth hormone deficiency, wherein treatment with rhGH increased the mean lean body mass, and decreased the fat mass; while in the group treated with growth hormone, neither changes significantly in the placebo group. Further, the basal metabolic rate, measured at base line and after one and six months of rhGH administration, increased significantly. Also, fasting plasma cholesterol levels were lower in the rhGH-treated group than the placebo group, whereas plasma triglyceride values were similar in the two groups throughout the study. Hence, in adults with growth hormone deficiency, six months of treatment with rhGH had a marked effect on body composition, resulting in an increase in lean body mass and a decrease in fat mass (See e.g., abstract, Figures, Tables and pages 1801-1802).

Thus, clearly demonstrating favorable effects of rhGH on the multiple perturbations associated with abdominal/visceral obesity, and as such, Applicant has not shown that the various growth hormones disclosed would be used in the manner claimed; except for the rhGH exemplified.

Therefore, in view of the above, the scope of treatment of a method comprising administering to said patient all kinds of growth hormones or functional derivatives thereof as claimed in independent claim 22 would involve tests for various growth hormones in all kinds of situations (i.e., there is no adequate disclosure in the instant specification to show the broad spectrum of administering growth hormone or a functional derivative thereof claimed intended for treating a patient having Metabolic Syndrome comprising Primary Insulin Resistance and abdominal/visceral obesity to decrease insulin resistance as claimed in claim 22). It would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since administration of numerous growth hormones or functional derivatives thereof are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which are not clearly disclosed. Thus, one of ordinary skill in the art would not be able to show that all treatment conditions as well as administration of all kinds of growth hormones or derivatives thereof are encompassed in the claims would be used as claimed in independent claim 22 in the instant invention. Thus, Applicant has not established any *nexus* between the various claimed growth hormones or functional derivatives thereof and their use in the manner claimed in claim 22.

Further, the first paragraph of 35 U.S.C. 112 requires, inter alia, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed

invention without undue experimentation. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicant is not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, in view of the above, and in view of the fact that there is no enablement in the instant specification for all kinds of growth hormones or functional derivatives thereof as well as method of treatment using the various growth hormones claimed thereof. Thus, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims for the reasons given above. Hence, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data and the breadth of the claims; the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence

commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 41 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 and 23 are indefinite and inconsistent in the recitation "functional derivative thereof" and "functional analog thereof", respectively. Although, on page 3, lines 19-20 in the instant specification "analog" is defined as a substance having the same biological activity as described here and having at least 65% homology with natural growth hormone; however, it is not clear or defined what is meant by "a functional derivative thereof" (claim 22) as well as "a functional analog thereof" (claim 23), and as such render the claims indefinite as to the claims metes and bounds.

Claim 24 is indefinite in the recitation "grown hormone". It is believed to be typographical error. Appropriate correction is required.

OBJECTION TO A CLAIM, ALLOWABLE SUBJECT MATTER

5. Claim 41 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The appropriate fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Mohamed/AAM

June 11, 2003

CHRISTOPHER S. F. LOW
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